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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,808	09/22/2004	Robert J. Etches	700603.7/1	3921

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,808	ETCHES ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *CRF Problem Report*.

DETAILED ACTION

Claims 1-9, 19 and 20 have been canceled. Claims 10-18 remain pending and under consideration.

Applicant's arguments filed 8-7-07 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendment to the specification filed 7-13-07 has not been entered because it does not mark the additions with underlining. In addition, the Cμ and Cδ symbols are missing on pg 31.

The sequence listing filed 7-13-07 was not saved in ASCII text. Applicants must submit a new sequence listing ASCII text. See attached CRF Problem Report.

Accordingly, this application still contains sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), **but the sequences throughout the specification do not include SEQ ID NOs. See pg 32, lines 1-5; pg 35, lines 10-11, pg 36, lines 8-9; pg 42, lines 6-9; pg 42, lines 16-24; pg 43, line 1; pg 43, lines 16-20**. Applicants must file a "Sequence Listing" accompanied by directions to enter the listing into the specification as an amendment. Applicant also must provide statements regarding sameness and new matter with regards to the CRF and the "Sequence Listing."

Claim Rejections - 35 USC § 112

The rejection of claim 19 under 35 U.S.C. 112, first paragraph, enablement has been withdrawn because the claim has been canceled.

Written Description

The rejection of claim 19 under 35 U.S.C. 112, first paragraph, written description has been withdrawn because the claim has been canceled.

Indefiniteness

Claims 10-18 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 remains indefinite because the phrase "wherein a population of B lymphocytes of the chicken are comprised of a human immunoglobulin locus encoding a human immunoglobulin heavy or light chain immunoglobulin molecule" remains unclear. A B cell can comprise a human gene but cannot comprise a human chromosome position as claimed. The amendment does not clarify the problem. B-lymphocytes do not "comprise" a "locus" i.e. a chromosome position. The position of the gene, i.e. the locus, does not describe the structure or function of the B-lymphocytes.

The phrase "pseudo" in claims 15 and 18 remains indefinite. It cannot be determined how "like" a human heavy chain V region a gene must be to be a "pseudo V gene" for example. Applicants argue the phrase is consistent with the phrase used in the prior art. Applicants' argument is unfounded. The phrase is not defined in the prior art.

Claim 16 remains indefinite because the structure of the resulting IgG molecule after switching cannot be determined. In addition, it cannot be determine what applicants consider "class switching." The distinction between rearrangement and switching cannot be determined. Ultimately, the structure of the "isotype G immunoglobulin molecules" in the B-cells cannot be determined. Applicants argue the phrase is consistent with the phrase used in the prior art. Applicants' argument is unfounded. The phrase is not defined in the prior art so that the structure of the isotype G immunoglobulin molecules in the B-cells can be determined.

The rejection regarding the metes and bounds of what applicants consider a "B lymphocyte specific regulatory region" (claim 19) has been withdrawn because the claim has been canceled.

Claim Rejections - 35 USC § 102

The rejection of claims 10-18 under 35 U.S.C. 102(e) as being anticipated by Etches (US Patent 6,861,572) has been withdrawn because '572 did not teach the transgene was stably integrated into the genome of the chicken.

Claims 10-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Rapp (Patent Application Publication US 2002/0108132 A1) for reasons of record.

Rapp taught a transgenic chicken whose genome comprised a transgene encoding a human heavy and/or light chain antibody comprising the V, D, C and J regions (paragraphs 63, 76, 151, 154, 161, 163).

The phrase "wherein a population of B lymphocytes of the chicken are comprised of a human immunoglobulin locus" in claim 10 does not make sense because B

lymphocytes cannot comprise a locus as claimed. A locus is a position on a chromosome; thus, a B-cell cannot comprise a position as claimed (see 112/2nd). It is noted that if the phrase is intended to mean the B-cells comprise a human immunoglobulin coding sequence, the B-cells of Rapp inherently comprise a human immunoglobulin coding sequence because the transgene encoding the human immunoglobulin is part of the chicken's genome (paragraph 76).

If claim 10 is intended to limit the transgenic chicken to a knock-in transgenic chicken, Rapp described making a knock-in transgenic chicken in paragraphs 80 and 121.

Claims 12-15 and 18 are included because the transgene may comprise a plurality of heavy or light chain V or D regions (paragraph 154). Claims 15 and 18 are included because the human immunoglobulin transgene is "like" the chicken immunoglobulin gene, i.e. "pseudo". The instant application does not define pseudo genes, thus leaving the meaning open to any reasonable interpretation.

Claim 16 is included because the B cells of the chicken inherently undergo immunoglobulin gene rearrangement class switching and yield isotype G immunoglobulin molecules because the transgene of Rapp encoded an entire heavy or light immunoglobulin chain that inherently comprised the switch region. Without evidence to the contrary, the transgene taught by Rapp has the function of claim 16. The structure of the transgenic chicken in claim 16 is not distinguished over the structure of the transgenic chicken described by Rapp.

Claim 17 is included because the antibody was expressed in the yolk of an egg produced by the chicken (paragraph 108).

Claim 18 is included because Rapp used the CMV promoter to express the transgene, which inherently expressed the transgene in all tissues, specifically in B-lymphocytes as claimed. The structure of the "B lymphocyte specific regulatory region" in claim 18 is not distinguished by structure or function over the CMV promoter described by Rapp.

Applicants' arguments have been considered but do not clearly set forth a difference between the claimed invention and the disclosure of Rapp. All limitations claimed have been specifically addressed in the rejection.

Claims 10-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Buelow (US Patent 7129084) for reasons of record.

Buelow taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Buelow taught a BAC vector with a chicken light chain modified by homologous recombination (Fig. 13-15). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene (Examples 12-14). The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy chain gene (col. 26, Example 11). Chimeric chickens were obtained (col. 27, line 44).

Applicants argue the reference is not enabling. Applicants' argument is not persuasive. The steps taught by Buelow are those required to make the chimeric chicken now claimed. All that is required in applicants' claim is the production of a chimeric chicken, which was well within the ability of the ordinary artisan.

Claims 10-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Singh (US Patent Application Publication 2002/0028488) for reasons of record.

Singh taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Singh taught a vector with a chicken light and heavy chain modified by homologous recombination (Fig. 2-4). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene. The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy or light chain gene (pg 8, paragraph 84).

Applicants' argue Singh did not enable the claimed invention. Applicants' argument is unfounded. Singh taught the method steps required to obtain the chimeric chicken claimed. It is unclear why applicants believe the reference is not enabled. It is unclear what specific method steps are lacking from Singh or why those of skill would not be able to apply the teachings of Singh to the chicken genome.

Double Patenting

Claims 10-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending

Application No. 11/062325 for reasons of record. Claim 8-11 of '325 are drawn to a genetically modified chicken expressing in tubular gland cells monoclonal antibodies encoded by an exogenous polynucleotide, wherein the monoclonal antibodies are present in egg white at a concentration of at least 40 .mu.g/ml. The product claimed in '325 is an obvious variant of the product claimed in the instant application and is described in the instant disclosure. The product claimed in this application is obvious in view of the claims of '089 taken with the disclosure of '089. This is a provisional obviousness-type double patenting rejection.

Claims 10-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/524089 for reasons of record. Claim 1-8 of '089 are drawn to A chicken selectively expressing exogenous protein in tubular gland cells wherein the protein is encoded by a transgene stably integrated into a genome of the chicken and wherein the transgene is comprised at least a portion of a promoter of a gene encoding an egg white protein that is operably linked to DNA encoding the exogenous protein. The product claimed in '089 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '089. The product claimed in this application is obvious in view of the claims of '089 taken with the disclosure of '089. This is a provisional obviousness-type double patenting rejection.

Claims 10-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-10 of copending Application No. 10/216098 for reasons of record. Claim 9-10 of '098 are

drawn to a chimeric chicken selectively expressing exogenous protein in tubular gland cells, wherein the exogenous protein is encoded by a transgene stably integrated into a genome of a donor embryonic stem cell whose progeny contribute to the chimeric chicken, and wherein the transgene is greater than 15 kb in size and is comprised of an at least a 7.5 kb portion of an ovalbumin promoter operably linked to DNA encoding the exogenous protein. The product claimed in '098 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '098. The product claimed in this application is obvious in view of the claims of '098 taken with the disclosure of '098. This is a provisional obviousness-type double patenting rejection.

Claims 10-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7 and 9 of US Patent 6,861,572 for reasons of record. Claim 1, 7 and 9 of '572 are drawn to an egg-laying chicken whose somatic cells contain an expression system comprising (i) a first DNA sequence encoding a human gamma isotype immunoglobulin constant region having a CH2-CH3 region in an Fc domain of the constant region; (ii) a second DNA sequence encoding a human immunoglobulin variable region; (iii) a third DNA sequence comprising an immunoglobulin-gene derived promoter sufficient for expression of the human immunoglobulin constant region in the chicken; wherein the egg-laying chicken produces eggs whose yolk contains human gamma isotype immunoglobulin having a constant region encoded by the first DNA sequence and a variable region encoded by the second DNA sequence. The product claimed in '572 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '572. The

product claimed in this application is obvious in view of the claims of '572 taken with the disclosure of '572.

Claim 12 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 14. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicants have not responded to any of the double patenting rejections.

Conclusion

The prior art made of record and not relied upon remains pertinent to applicant's disclosure:

MacArthur (WO 97/47739)

MacArthur (US Patent 6,825,396, Nov. 30, 2004, filed 4-18-97)

Davis (Bio/Technology, Feb. 1991, Vol. 9, pg 165-169)

Etches, US Patent Application 10/067148 now US Patent 7,145,057.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER

SCORE

CRF Problem Report

SCORE experienced a problem when processing the following computer readable form (CRF):

Application Serial Number: 10506806
Filing Date: 7/18/07
Date Processed by SCORE: 6/7/07

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Revised 01/20/06